October 20, 1958

Dr. Herman Kalckar
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Dear Herman:

To your note of October 10th. It is most interesting that your galactose-inhibited cultures are killed by penicillin without undergoing lysis. I can only say from our own experience that bacteriostasis which results from nutritional deficiency, inhibition by chloramphenicol, or low temperature, will protect against the lytic effects of penicillin. It seems to me less important to find ways in which the protection by galactose can be overcome than to study the mechanism of killing more closely. Will the cells be restored by removing galactose and replacing this with glucose? Will they undergo lysis on dilution into distilled water?

My only thought about mechanism is that perhaps you should consider this as a penicillin-induced sensitivity to galactose rather than the other way around. For example, cell wall formation might be a pathway that could divert appreciable amounts of galactose-1-phosphate and if this pathway is blocked by penicillin you may then have a more toxic effect of the accumulated intermediate. The fact that you do not get lysis seems to me indicative of a mechanism of killing altogether different from that of penicillin. You might be able to test this by using resting suspensions which should still be able to metabolize galactose and accumulate toxic intermediates.

Is the inhibition confined to the effect of intracellular gal-1-p or can you duplicate it by adding gal-1-p to the medium?

As ever,